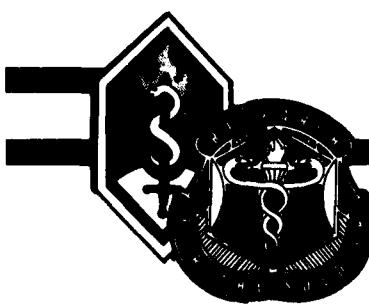


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USAARL Report No. 88-4

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Comparison of Three Anesthetics for Chinchilla

By

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Sensory Research Division

April 1988

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REPORT DOCUMENTATION PAGE			
1a. REPORT SECURITY CLASSIFICATION Unclassified		1b. RESTRICTIVE MARKINGS	
2a. SECURITY CLASSIFICATION AUTHORITY		3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution unlimited	
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE			
4. PERFORMING ORGANIZATION REPORT NUMBER(S) USAARL Report No. 88-4		5. MONITORING ORGANIZATION REPORT NUMBER(S)	
6a. NAME OF PERFORMING ORGANIZATION U.S. Army Aeromedical Research Laboratory	6b. OFFICE SYMBOL (if applicable) SGRD-UAS-AS	7a. NAME OF MONITORING ORGANIZATION U.S. Army Medical Research and Development Command	
6c. ADDRESS (City, State, and ZIP Code) Fort Rucker, AL 36362-5292		7b. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, MD 21701-5012	
8a. NAME OF FUNDING/SPONSORING ORGANIZATION	8b. OFFICE SYMBOL (if applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER	
8c. ADDRESS (City, State, and ZIP Code)		10. SOURCE OF FUNDING NUMBERS	
		PROGRAM ELEMENT NO. 61102A	PROJECT NO. 3M1611 02BS15
		TASK NO. CB	WORK UNIT ACCESSION NO. 282
11. TITLE (Include Security Classification) Comparison of Three Anesthetics for Chinchilla (U)			
12. PERSONAL AUTHOR(S) C.E. Hargett, Jr., Ilia M. Lomba-Gautier, Melvin Carrier, Jr., Carol S. Landon, Irving W. McConnell, James H. Patterson, Jr.			
13a. TYPE OF REPORT Final	13b. TIME COVERED FROM _____ TO _____	14. DATE OF REPORT (Year, Month, Day) 1988 April	15. PAGE COUNT 19
16. SUPPLEMENTARY NOTATION			
17. COSATI CODES	18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number) Chinchilla >Ketamine; Xylazine; Acepromazine; Anesthesia; (K) ←		
19. ABSTRACT (Continue on reverse if necessary and identify by block number) Anesthesia techniques which successfully induce surgical anesthesia in Chinchilla vellidera are described and compared. Two injectables, ketamine-acepromazine and ketamine-xylazine, are compared to halothane-nitrous oxide administered by mask only and the same mixture administered by induction chamber until loss of righting reflex and then mask. Forty laboratory-raised adult chinchillas in four groups were used in this study. Subjects were weighed and dosages calculated and administered. All achieved surgical anesthesia with no deaths. Time to loss of righting reflex, time to surgical anesthesia, duration of surgical anesthesia, time from end of surgical anesthesia to standing unaided, and total time from administration of anesthesia to standing unaided are detailed. Findings indicate that the doses evaluated of ketamine-acepromazine, ketamine-xylazine, and halothane-nitrous oxide all provide safe, dependable surgical anesthesia.			
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input checked="" type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION Unclassified		
22a. NAME OF RESPONSIBLE INDIVIDUAL Chief, Scientific Information Center	22b. TELEPHONE (Include Area Code) (205) 255-6907	22c. OFFICE SYMBOL SGRD-UAX-SI	

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Acknowledgments

This work was supported by the U.S. Army Medical Research and Development Command (USAMRDC) under Contract Number DAMD17-86-C-6139.

C.E. Hargett, Jr., an employee of the Research Foundation, State University of New York at Plattsburgh, is assigned full-time at the U.S. Army Aeromedical Research Laboratory (USAARL) as part of the above contract.

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The views of the authors do not purport to reflect the positions of the Department of the Army or the Department of Defense.

In conducting research using animals, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (NIH Publication 86-23, revised 1985).

The authors wish to acknowledge and thank Ms. Linda S. Barlow for her valuable statistical assistance.

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Introduction

The chinchilla (*Chinchilla vilidera*) is the animal model of choice for certain types of auditory research (Miller, 1970). The Acoustical Sciences Branch, Sensory Research Division of the U.S. Army Aeromedical Research Laboratory (USAARL), Fort Rucker, Alabama, has used the chinchilla as a research animal model since 1977 (Burdick, et al., 1978).

In auditory research, it is necessary to perform surgical procedures such as monauralizations and electrode implants as part of acoustical experimentation. This requires an acceptable method of anesthetizing the animals. Relatively few studies have been reported documenting the use of anesthetics in the chinchilla. Intramuscular injections of ketamine-acepromazine have been used successfully by some research teams (Morgan, et al., 1981). Ketamine is a nonbarbiturate that rapidly produces a cataleptic state of anesthesia characterized as disassociate anesthesia. Acepromazine has a depressant effect on the central nervous system. While anesthesia is rapid with this combination, recovery tends to be slow. In one study, the duration of surgical anesthesia exceeded 40 minutes and required 120 to 300 minutes for complete recovery (Morgan, et al., 1981).

There were no references in the literature that we found to ketamine-xylazine combinations used to anesthetize chinchillas. CI-744 (tiletamine-HCL and zolezepan-HCL) was reported to be effective for chinchilla anesthesia with a mean duration of 202 minutes for five animals given the minimum dosage (22 mg/kg) that provides surgical anesthesia (Schultz and Fowler, 1974). Xylazine is an alternative to acepromazine.

Experience at USAARL has shown that 20 to 25 minutes of surgical anesthesia is sufficient for most procedures. For this reason, a mixture of halothane and nitrous oxide has been used to anesthetize our chinchillas for surgery. Halothane is a halogenated hydrocarbon that produces a potent nonexplosive anesthesia agent (Deutsch, 1978). Inhalation anesthesia has a number of advantages. The agents are eliminated primarily through the lungs, so recovery from anesthesia does not rely upon redistribution within the body and detoxification mechanisms (Lumb and Jones, 1973). Halothane is a "complete anesthetic" capable of producing surgical anesthesia without oxygen deprivation and is nonirritating to the upper and lower respiratory tracts (Deutsch, 1971). Salivary, mucous, and bronchial secretions, as well as laryngospasms and vomiting, are not problems when using halothane anesthesia. Nitrous oxide is used with halothane to provide rapid induction, analgesia, and to complement the more potent anesthetic agent (Lumb and Jones, 1973; Soma, 1971). Inhalation anesthesia requires specialized equipment, but it is the only technique that allows for control

of anesthetic depth and surgical anesthesia duration. The present study was undertaken to compare halothane anesthesia with ketamine in combination with either acepromazine or xylazine. In addition, two methods for inducing halothane anesthesia were compared.

Methods and procedures

This study utilized 40 healthy chinchillas of both sexes from the USAARL colony. Individual stainless steel laboratory cages (483mm x 607mm x 203mm) were used as housing for these chinchillas. They were provided with commercial chinchilla ration* and water ad libitum. They weighed from 375.2 grams to 643.1 grams with a mean weight of 496.1 grams and a median weight of 487.2 grams. Ages ranged from 10 to 48 months. They were assigned randomly to four groups of 10 subjects each. The chinchillas were not deprived of food or water prior to the experiment and were returned to individual cages upon being able to stand unaided.

Each subject was anesthetized to surgical depth by the method of anesthesia for its assigned group. Surgical depth is defined as not exhibiting pedal reflex, or palpebral reflex, and is corroborated by subjective observations evaluating the chinchilla's overall appearance and condition. On each subject, we collected the following data: respiration rates, time to loss of righting reflex, time to loss of palpebral reflex, time to loss of pedal reflex, time at surgical depth, time to return of pedal reflex, and time to standing unaided. Time to head lift from lateral recumbency and both pinna and whisker reflex were taken on some of the injectable subjects. However, it was not possible to acquire these data on the gas anesthesia subjects as the mask is in place providing oxygen flow at the time these reflexes occur. Time at surgical depth for the inhalation anesthesia subjects was limited to 20 minutes for the purposes of this report. This is not to be taken as an upper time limit for this technique, merely the time we find to be optimal for our surgical techniques.

The four methods used to induce surgical anesthesia were:

Group I: Halothane* and nitrous oxide administered by the mask only.

Group II: Halothane and nitrous oxide administered by the anesthesia chamber until loss of righting reflex, then by the mask.

*See Appendix A.

Group III: Ketamine*-acepromazine administered by injection.

Group IV: Ketamine-xylazine* administered by injection.

All times were taken with a stopwatch and recorded as the nearest minute and second, except duration of surgical depth and time to standing unaided for Groups III and IV, which were taken to the nearest minute.

The long duration of the effects of the injections make time rounded to the nearest whole minute more appropriate. Statistical tests of the equivalence of means across the four groups were accomplished using a one-way analysis of variance followed by a posteriori comparisons using Tukey's honestly significant differences (Winer, 1971). A separate analysis was done for each dependent variable.

Group I

Ten chinchillas with a mean weight of 522.6 grams were anesthetized using a mask-only system of inhalation anesthesia. The mask system is a nonrebreathing system. It is well-suited for smaller animals such as a chinchilla. The chinchillas were picked up from the transport cage, placed on the surface of the Narkivet* anesthesia machine and their heads inserted into the mask. They were held with heads in the mask until loss of righting reflex occurred. A 4 percent setting of halothane, with a flow rate of 4 liters per minute of nitrous oxide and 2 liters per minute of oxygen, was used.

When the palpebral reflex was gone, the chinchilla was removed from the mask and Optivet* chloramphenicol eye ointment was placed in each eye, and the eyes were closed. This kept the eye tissue from drying out. Then, the subject was returned to the mask. The loss of pedal reflex was taken as beginning of surgical depth. The chinchilla was maintained at surgical depth using a 2 1/2 percent halothane setting, with a flow rate of 2 liters per minute of nitrous oxide and 2 liters per minute of oxygen.

At the end of the procedure, the halothane was set at 0 percent (no flow), the nitrous oxide at zero liters per minute (no flow) and the oxygen maintained at 2 liters per minute. This enabled the chinchilla to return to consciousness rapidly, without complications induced by nitrous oxide (Soma, 1971).

Group II

Ten chinchillas with a mean weight of 459.6 grams were anesthetized using a precharged Ejay* international anesthesia chamber. It is made of tough, lightweight, transparent plastic. This chamber is supposed to reduce the stress on the subject prior to being anesthetized. The unit was precharged with halothane-nitrous oxide. Then the chinchilla was inserted and the lid quickly closed. The chamber is transparent, so ataxia could be observed.

Gently shaking the unit would cause the chinchilla to topple over at the onset of loss of righting reflex. At the loss of righting reflex, the chinchilla was removed from the unit, tested for palpebral reflex, eyes filled with Optivet ointment, and placed on the mask that is attached to the Narkovet anesthesia machine. At this point, all further details were the same as for subjects in Group I.

Group III

Ten chinchillas with a mean weight of 513.6 grams were injected intramuscularly in the left gluteal area with a mixture of ketamine hydrochloride (40 mg/kg) and acepromazine (approximately 0.5 mg/kg) using the technique described by Morgan et al., 1981.

Subjects were weighed and individual doses calculated and drawn up into a 1 cc tuberculin syringe. Upon injection, subjects were placed in a 457 mm x 304 mm x 228 mm transparent plastic box for observation.

At loss of righting reflex, subjects were tested for palpebral reflex and then eyes were filled with Optivet ointment and closed to prevent drying. Then, subjects were placed in a recumbent position for further observations.

Group IV

Ten chinchillas with a mean weight of 488.7 grams were injected in the left gluteal area with a mixture of ketamine hydrochloride (40 mg/kg) and xylazine (2 mg/kg). After calculating the dosage of ketamine to be injected, this dosage was drawn into a 1 cc tuberculin syringe, then cleared of air bubbles. This syringe was inserted into the xylazine vial and the calculated dosage of xylazine drawn on top of the ketamine. Next, air was drawn into the syringe and the two agents well blended. All the air was expelled and then the blend of ketamine-xylazine was injected. Upon injection, subjects were placed in a 457mm x 304 mm x 228 mm transparent plastic box for observation.

Results and Discussion

The times to loss of righting reflex are shown in Table 1. The analysis of variance revealed significant differences ($\alpha = .05$) in mean time to loss of righting reflex among the four groups. However, a posteriori analysis failed to find any differences between individual groups.

Table 1

Time to loss of righting reflex in seconds

	<u>Group I</u>	<u>Group II</u>	<u>Group III</u>	<u>Group IV</u>
Median	128.5	117.5	87.5	85.0
Range	(46-170)	(60-205)	(72-135)	(61-124)
Average	124.1	129.4	94.9	86.8
S.D.	34.3	54.9	22.6	20.5

Group I = Mask only

Group II = Induction chamber, then mask

Group III = Ketamine-acepromazine

Group IV = Ketamine-xylazine

Table 2 shows the time to surgical anesthesia in seconds. The time to surgical anesthesia was shortest for the ketamine-xylazine combination; both gas techniques required about the same time. The ketamine-acepromazine combination yielded the longest time to surgical depth. The slowest subject to reach surgical anesthesia (no pedal reflex, no palpebral reflex) in this group took 723 seconds (just over 12 minutes). The analysis of variance showed a significant difference ($\alpha = .05$) between groups. The a posteriori analysis revealed significant differences between Group IV and both Groups I and II, and between Group III and the other groups. No significant difference existed between Groups I and II.

Table 2

Time to surgical anesthesia in seconds

	<u>Group I</u>	<u>Group II</u>	<u>Group III</u>	<u>Group IV</u>
Median	332.5	298.0	455.5	203.0
Range	(150-402)	(230-445)	(324-723)	(121-311)
Average	308.2	298.8	481.8	197.7
S.D.	72.7	67.6	123.6	453.4

Group I = Mask only

Group II = Induction chamber, then mask

Group III = Ketamine-acepromazine

Group IV = Ketamine-xylazine

The durations of surgical anesthesia are shown in Table 3. The time at surgical anesthesia can best be controlled by use of a gas anesthesia machine. If using injectables, once administered, the rate at which the agent is metabolized is the major factor. Although additional doses can be given to increase time at surgical depth, this method is not as readily controlled as with the gas machine. The average time for Group III (ketamine-acepromazine) to be at surgical anesthesia was 54.4 minutes while for Group IV (ketamine-xylazine) it was 121.8 minutes. Both Groups I and II (gas techniques) began to recover fairly rapidly as soon as there was no flow of both halothane and nitrous oxide and oxygen remained at 2 liters per minute. The analysis of variance showed a significant difference between groups. Significant differences between Group IV and Groups I and II, and Group III were found with the *a posteriori* analysis. The difference between Groups I and II was not significant.

Table 3

Duration of surgical anesthesia in minutes

	<u>Group I</u>	<u>Group II</u>	<u>Group III</u>	<u>Group IV</u>
Median	24.5	25.0	58.0	114.5
Range	(24-26)	(23-26)	(30-82)	(103-153)
Average	24.6	24.7	54.4	121.8
S.D.	0.7	1.0	16.7	16.8

Group I = Mask only

Group II = Induction chamber, then mask

Group III = Ketamine-acepromazine

Group IV = Ketamine-xylazine

One of the major considerations is the total time from the end of surgical depth anesthesia to complete recovery, determined as the time to standing unaided shown in Table 4. Groups I and II showed very rapid recovery with an average of 8.2 and 9.5 minutes, respectively. As expected, there was no statistical difference between the two gas methods. Group III (ketamine-acepromazine) showed an average time of 81.3 minutes and Group IV (ketamine-xylazine) showed an average time of 55.8 minutes. These are significantly different from each other and from Groups I and II. Rapid recovery is one of the primary advantages of the gas anesthesia method.

Table 4

Minutes from end of surgical anesthesia to standing unaided

	<u>Group I</u>	<u>Group II</u>	<u>Group III</u>	<u>Group IV</u>
Median	7.3	9.2	65.0	51.5
Range	(4.2-16.0)	(7.3-12.3)	(52-135)	(23-97)
Average	8.2	9.5	81.3	55.8
S.D.	3.2	1.7	32.9	26.1

Group I = Mask only

Group II = Induction chamber, then mask

Group III = Ketamine-acepromazine

Group IV = Ketamine-xylazine

Table 5 summarizes the total time from administration of anesthesia to standing unaided, defined as complete recovery. The average for this measure was over 100 minutes longer with injectables than the worst of the two gas methods. The analysis of variance showed a significant difference between groups. The a posteriori analysis revealed differences between Group IV, Groups I and II, and Group III. No significant difference between Groups I and II was found.

Table 5

Time from administration of anesthesia to standing unaided

	<u>Group I</u>	<u>Group II</u>	<u>Group III</u>	<u>Group IV</u>
Median	32.0	34.0	121.5	178.5
Range	(30-47)	(31-39)	(83-216)	(138-231)
Average	33.8	34.4	135.7	180.4
S.D.	4.9	2.6	42.1	32.8

Group I = Mask only

Group II = Induction chamber, then mask

Group III = Ketamine-acepromazine

Group IV = Ketamine-xylazine

Conclusion

Although each of the four methods of anesthesia will provide a satisfactory depth and duration of surgical anesthesia, there are advantages to each. Our findings with ketamine-acepromazine injected IM are in general agreement with those of Morgan, et al., 1981. They reported an induction period of about 5 minutes. We found a range of about 5-12 minutes with an average of 5.2 minutes. They reported surgical anesthesia lasting from 40-60 minutes. We found a range of 30-82 minutes with an average of 54.4 minutes. They reported

complete recovery in 2-5 hours. We found a range of 1.4-3.6 hours with an average of 2.3 hours from injection until the subject could stand unaided.

The injectables are less controllable once the ketamine-acepromazine or ketamine-xylazine is administered and have a long duration from injection to complete recovery. The ease of administering gas is apparent, but so is the initial expense of procuring the anesthesia unit. The use of the anesthesia chamber allows a smoother induction of anesthesia with minimal stress to the subject, but the subject must be removed from the anesthesia chamber and placed on the mask. This results in loss of gas anesthesia from the chamber. Then the chamber must be precharged again for each subsequent subject. With the ketamine combination injections, time to loss of righting reflex is somewhat shorter. The ketamine-xylazine has the shortest time to loss of righting reflex and to surgical anesthesia, however duration of surgical depth and time to complete recovery are excessive for our needs. On the other hand, time at surgical depth can be controlled with either gas method, minimizing the time at surgical depth.

We conclude that for situations requiring control over length of anesthesia and rapid recovery from anesthesia, either inhalation technique is superior to either ketamine-acepromazine or ketamine-xylazine injections, with the anesthesia chamber minimizing stress on the individual subjects.

Appendix A
List of Manufacturers

Ralston Purina Company
Checkerboard Square
St. Louis, MO 63164
(Purina Chin Chow)

Halocarbon Laboratories, Incorporated
82 Berlews Court
Hackensack, NJ 07601
(Halothane U.S.P.)

Bristol Laboratories
Division of Bristol-Myers Company
Syracuse, NY 13201
(Ketaset)

CEVA Laboratories, Incorporated
Overland Park, KS 66212
(Acepromazine)

Bayvet Division
Miles Laboratories, Incorporated
Shawnee, KS 66201
(Rompum)

North American Drager
148B Quarry Road
Telford, PA 18969
(Narkovet)

Burns-Biotec Laboratories, Incorporated
8536 K Street
Omaha, NE 68127
(Optivet)

Ejay International, Incorporated
P.O. Box 1835
Glendora, CA 91740
(Ejay)

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